Wyeth

Wyeth Pharmaceuticals

Date: October 21, 2005

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2005D-0288: August 8, 2005 (70 FR 45722-45723)

Dear Sir/Madam:

Wyeth Pharmaceuticals is submitting the following comments on the draft guidance for industry entitled, *ICH Q9 Quality Risk Management.*

Wyeth is one of the largest research-based pharmaceutical and healthcare products companies and is a leading developer, manufacturer and marketer of prescription drugs, biopharmaceuticals, vaccines, and over the counter medications.

Wyeth appreciates the opportunity to comment on the above-mentioned draft ICH guidance; our comments are provided below

Comment 1

- The following terms are used throughout the document: *process*, *residual risk* and *safety* in the document. For clarity we recommend that they be defined and included in the glossary. Listed below are recommended definitions from other international risk management standards:

  Process: A set of inter-related resources and activities that transform inputs into outputs. (Ref: ISO 8402)

  Residual Risk: Risk remaining after protective measures have been taken. (Ref: ISO/IEC 51)

  Safety: Freedom from unacceptable risk (Ref: ISO/IEC 51)

Comment 2

- We recommend that the definition for *risk reduction* be expanded. See italicized text below.

  Risk Reduction: Actions taken either to lessen the probability of occurrence of harm or the severity of that harm, *or to increase the likelihood of detection of a risk-related problem.*

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Comment 3

- For linkage to ICH Q8, Pharmaceutical Development, more detail is needed in ICH Q9 regarding the hierarchy of options available for risk reduction. Other international risk management standards (e.g., ISO/IEC 14971 and IEC 60601-1-4) and FDA medical device submission guidance provide the following categories for risk reduction:

  1. Eliminate or reduce the risk by inherent safe design (or redesign)
  2. Reduce the risk by protective measures, and
  3. Reduce the risk by adequate user information, such as warnings

  Where technically viable, designing for inherent safety is the preferred approach. When that is not possible, the next alternative is to provide protective measures (e.g., alarms, special quality checks, redundancy, special processing procedures, etc.). After design and protective measures are exhausted, any remaining residual risk should be reduced to an acceptable level through providing information and warnings. This (or a similar) hierarchy of risk reduction approaches should be described and further explained in the document.

Comment 4

- Other international risk standards (e.g., ISO/IEC 14971 and IEC 60601-1-4) describe a three level risk categorization:

  1. Intolerable
  2. ALARP (As Low As Reasonably Practicable)
  3. Broadly Acceptable

  This three-level approach (with the concept of ALARP) has been helpful in other industries, and has been recognized by FDA through its standards recognition program, but it was not incorporated in the ICH Q9 guide. Either in the ICH document or in the preamble, it would be helpful to include some further explanation as to why this approach was not selected.

Comment 5

- Risk control measures need to be verified to assure they actually work and achieve the desired level of protection. They should be a focus of attention during system qualification, process validation and other quality activities. Such verification should be covered as an inherent part of Risk Control – not just under Risk Review as described in the draft.

Comment 6

- The draft guidance does not differentiate software failure from systematic defects. Defects of software tend to be dependant upon specific conditions and are not due to random life-span events such as hardware failure. Typically, one regards probability and severity as the risk attributes for ranking. When the failure is systematic, probability has no role since probability equals 1. Therefore, without discussion of this issue, users may factor probability for situations where probability should not be included.

Wyeth

We are submitting the enclosed comments in duplicate. Again, Wyeth appreciates the opportunity to comment on the above-mentioned draft guidance, and trusts that the Agency will take these comments into consideration.

Sincerely,

Roy J. Baranello
Assistant Vice President
Regulatory Policy & Operations